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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/027,671	02/23/1998	ALAN K. SMITH	4292-0048-55	3507

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EXAMINER	
BELYAVSKYI, MICHAIL A	
ART UNIT	**PAPER NUMBER**
1644	

NOTIFICATION DATE	DELIVERY MODE
03/31/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	09/027,671	SMITH ET AL.	
	Examiner	Art Unit	
	Michail A. Belyavskyi	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 February 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *95-132* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *95-132* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment filed on 02/08/08 is acknowledge

2. Claims 95-132 are pending.

Claims 95-132 read on method of obtaining human T cells with enhanced replicative function and cytokine secretion comprising culturing said human T cells in a liquid culture medium which is replaced at a rate of at least 50% to 100% daily for the cell are under consideration in the instant application.

In view of the amendment, filed 09/27/07 the following rejections remain:

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 95-132 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,994,126 and US Patent 5,290,700 for the same reasons set forth in the previous Office Action, mailed on 12/12/07.

Applicant's arguments, filed 02/08/08 have been fully considered, but have not been found convincing.

Applicant asserts that : (i) US Patent 126 does not describe or otherwise suggest culturing T cells as claimed; (ii) the results for T cells as shown in the specification are unexpected and novel, since conventional wisdom emphasizes splitting cultures to maintain low density.

Contrary to Applicant's assertion, it has been recently stated that KSR forecloses the argument that a specific teaching, suggestion, or motivation are required to support a finding of obviousness See Board decision (see *KSR International Co v Teleflex Inc.*, 550U.S.-, 82 USPQ2d 1385, 2007).

In the instant case, US Patent '126 teaches a method of obtaining lineage committed human cells comprising culturing said cells under physiologically acceptable liquid culture conditions including replacement of the liquid culture medium at a rate and for a time sufficient to obtained cells suitable for various immunological intervention and treatment of diseases and transferring said cultured cells into a patient (see entire document, column 12, lines 55-65, column 13, lines 10-25, column 15, line 54-65 and column 21, line 29-35 in particular). US Patent '126 teachers that media replaced every other day for about $5x10^5$ cells/ml culture(see column 17, lines 60-65 and Example 1 in particular). US Patent '126 teachers that culture medium is any culture medium suitable for growing human cells for example RPMI (see column 16, lines 15-65 and Examples 1 and 2 in particular) . It is noted that US Patent '126 teaches does not explicitly teaches that said cells are T cells or that said cells will have an enhanced replicative function or cytokine secretion as compared to the function of the cell cultured *ex-vivo* under conditions which do not include replacement of the liquid culture. However, it is noted that the referenced cells are human cells that have been cultured under the same culturing conditions as claimed thus obviously would have the same enhanced biological function *in vitro*. It is also noted that discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer. " The Court further held that "this same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art". See MPEP 2112.02. Also, see Bristol-Myers Squibb Co. v. Ben Venue Laboratories, Inc. 58 USPQ2d 1508 (CA FC 2001); Ex parte Novitski 26 USPQ 1389 (BPAI 1993); Mehl/Biophile International Corp. V. Milgraum, 52 USPQ2d 1303 (Fed. Cir. 1999); Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed.

UD Patent 5,290,700 teaches a method of culturing mammalian cell under conditions wherein the growth medium is constantly perused, i.e. constantly replaced (see entire document, Abstract in particular). US Patent'700 teaches that said culturing system make it possible to grow cell to high cell density , without the need of splitting the cells, for example up to $5x\ 10^8$ cell/ml (see column 1 in particular). It is noted that US Patent '700 does not explicitly disclosed culturing human T cell under said conditions. However, it is noted that the referenced cells are human cells that have been cultured under the same culturing conditions as claimed thus obviously would have the same enhanced biological function *in vitro*. It is also noted that discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to

the discoverer. " The Court further held that "this same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art". See MPEP 2112.02. Also, see Bristol-Myers Squibb Co. v. Ben Venue Laboratories, Inc. 58 USPQ2d 1508 (CA FC 2001); Ex parte Novitski 26 USPQ 1389 (BPAI 1993); Mehl/Biophile International Corp. V. Milgraum, 52 USPQ2d 1303 (Fed. Cir. 1999); Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed.

All the claimed elements were known in the prior art and one skill in the art could have combine the elements as claimed by known methods with no change in their respective function and the combination would have yield predictable results to one of ordinary skill in the art at the time of the invention (see *KSR International Co v Teleflex Inc.*, 550U.S.-, 82 USPQ2d 1385, 2007).

With regard to Applicant's statement that the results for T cells as shown in the specification are unexpected and novel, since conventional wisdom emphasizes splitting cultures to maintain low density.

The Examiner disagrees with said statement. As has been discussed above , at the time the invention was made one skill in the art would know that growing cells under condition wherein the growth medium is constantly perused, i.e. constantly replaced would make it possible to produce a cell culture with high cell density without the need of splitting cultures. Moreover, the fact that T cells grown under conditions wherein growth medium is replaced would have different biological function compare to cells that are cultured under static conditions would be quit expected to one skill in the art at the time the invention was made.
As had been discussed in the previous Office Action, in the Declaration by Dr. Smith submitted on 04/30/07 the cells growing under static culture (0% exchange) has been compared with cells growing under condition of continuously culture exchange (12, 25, 35 and 50 % exchange) on days 7, 12 and 19. In other words, cells that were grown up to 7, 12 or 19 days without medium exchange have been compared with cells grown under condition wherein culture medium has been constantly exchange. It is well know to one skilled in the art that maintaining cells under optimal growth conditions requires medium exchange on a daily basis and at appropriate cell density. (see for example Basic Cell Culture protocols, ed. Helgason and Miller, 2005, page 219). Moreover, in the Manual of Cell Culturing techniques ed. Stacey and Hockley, 2000, page 24) it is explicitly sated that maintaining cell under optimal growth conditions can be very difficult in tradition tissue culture flasks and **failure to provide adequate changes of culture medium** and failing to passage cells at appropriate times can **cause a range of deleterious effects in the cells** that might result in changes in the characteristics of the culture which may be permanent and **alter the response of cells in bioassays or other applications** (emphases added). In other words it would be well known to one skill in the art that cells growing under static condition (0% exchane) for more than 7, 12 or 19 days would have different biological function compare to cells grown under condition of continuously culture exchange.

Claims 114-132 are included because it would be conventional and within the skill of the art to determine the optimum concentration of sera or plasma and glucose, lactate ,glutamine and ammonia in the growth media, or type of T cells that can be incubated under claimed conditions or determine an optimal cell density . Further, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 220 F2d 454,456,105 USPQ 233; 235 (CCPA 1955). see MPEP § 2144.05 part II A.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

4. No claim is allowed.

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is 571/272-0840. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571/272-0841.

The fax number for the organization where this application or proceeding is assigned is 571/273-8300

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free)

/Michail A Belyavskyi/
Primary Examiner, Art Unit 1644